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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/784,900	02/24/2004	Eugene R. Cooper	029318-1003	1015

31049 7590 04/06/2009

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EXAMINER	
TRAN, SUSAN T	

ART UNIT	PAPER NUMBER
1615	

MAIL DATE	DELIVERY MODE
04/06/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/784,900	COOPER ET AL.	
	Examiner	Art Unit	
	S. Tran	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 December 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-72* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-72* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-72* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 01/15/09 has been entered.

Election/Restrictions

Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 1-25 and 50-72 are drawn to a nanoparticulate composition, classified in class 424, subclass 489 and 490.

II. Claims 26-49 are drawn to a method for preparing the nanoparticulate composition, classified in class 264, subclass 10.

The inventions are distinct, each from the other because of the following reasons:

Inventions I and II are related as process of making and product made. The inventions are distinct if either or both of the following can be shown: (1) that the process as claimed can be used to make another and materially different product or (2) that the product as claimed can be made by another and materially different process (MPEP § 806.05(f)). In the instant case, the product as claimed can be made by another and materially different process. The product of Group I does not require

contacting the meloxicam and surface modifier by grinding, homogenizing, or precipitating.

Restriction for examination purposes as indicated is proper because all these inventions listed in this action are independent or distinct for the reasons given above and there would be a serious search and examination burden if restriction were not required because one or more of the following reasons apply:

(a) the inventions have acquired a separate status in the art in view of their different classification;

(b) the inventions have acquired a separate status in the art due to their recognized divergent subject matter;

(c) the inventions require a different field of search (for example, searching different classes/subclasses or electronic resources, or employing different search queries);

(d) the prior art applicable to one invention would not likely be applicable to another invention;

(e) the inventions are likely to raise different non-prior art issues under 35 U.S.C. 101 and/or 35 U.S.C. 112, first paragraph.

Applicant is advised that the reply to this requirement to be complete must include (i) an election of a invention to be examined even though the requirement may be traversed (37 CFR 1.143) **and (ii) identification of the claims encompassing the elected invention**.

The election of an invention may be made with or without traverse. To reserve a right to petition, the election must be made with traverse. If the reply does not distinctly and specifically point out supposed errors in the restriction requirement, the election shall be treated as an election without traverse. Traversal must be presented at the time of election in order to be considered timely. Failure to timely traverse the requirement will result in the loss of right to petition under 37 CFR 1.144. If claims are added after the election, applicant must indicate which of these claims are readable on the elected invention.

If claims are added after the election, applicant must indicate which of these claims are readable upon the elected invention.

Should applicant traverse on the ground that the inventions are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the inventions to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. 103(a) of the other invention.

This application contains claims directed to the following patentably distinct species if the process of making is elected.

The process step of contacting meloxicam with at least one surface stabilizer by:

1) grinding;

2) wet grinding;

3) homogenizing; and

4) precipitating.

The species are independent or distinct because claims to the different species recite the mutually exclusive characteristics of such species. In addition, these species are not obvious variants of each other based on the current record.

Applicant is required under 35 U.S.C. 121 to elect a single disclosed species for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable. Currently, claim 26 is generic.

There is an examination and search burden for these patentably distinct species due to their mutually exclusive characteristics. The species require a different field of search (e.g., searching different classes/subclasses or electronic resources, or employing different search queries); and/or the prior art applicable to one species would not likely be applicable to another species; and/or the species are likely to raise different non-prior art issues under 35 U.S.C. 101 and/or 35 U.S.C. 112, first paragraph.

Applicant is advised that the reply to this requirement to be complete must include (i) an election of a species to be examined even though the requirement may be traversed (37 CFR 1.143) **and (ii) identification of the claims encompassing the elected species**, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered nonresponsive unless accompanied by an election.

The election of the species may be made with or without traverse. To preserve a right to petition, the election must be made with traverse. If the reply does not distinctly and specifically point out supposed errors in the election of species requirement, the

election shall be treated as an election without traverse. Traversal must be presented at the time of election in order to be considered timely. Failure to timely traverse the requirement will result in the loss of right to petition under 37 CFR 1.144. If claims are added after the election, applicant must indicate which of these claims are readable on the elected species.

Should applicant traverse on the ground that the species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the species unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. 103(a) of the other species.

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which depend from or otherwise require all the limitations of an allowable generic claim as provided by 37 CFR 1.141.

Claim Rejections - 35 USC § 103

Claims 1-17, 26-29, 31-42 and 50-67 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bosch et al. US 5,510,118, in view of Plachetka et al. US 6,479,551 or Struengmann et al. WO 99/09988 A1.

Bosch teaches a process of preparing nanoparticulate drug substances comprising the steps of dispersing a crystalline drug in a liquid dispersion medium containing a surface modifier, and subjecting the premix to mechanical means to reduce

the particles size of the drug substance to less than 400 nm (abstract; column 4, lines 3-10; and column 7, lines 40 through column 8, lines 1-40). Drug includes water-insoluble drug substance such as an NSAID substance (column 5, lines 1-2; and table 1). Surface modifier includes nonionic, anionic, organic, inorganic excipients, and mixture of two or more (column 5, lines 45 through column 6, lines 1-29). Bosch further teaches the surface modifier is adsorbed on the surface of the drug substance, but the individually adsorbed molecules of the surface modifier are essentially free of intermolecular crosslinkages (column 6, lines 29-35).

Bosch does not explicitly teach the claimed analgesic agent such as meloxicam.

Plachetka teaches long acting NSAID typically includes naproxen, and meloxicam (column 2, lines 62-66; and column 3, lines 54-60).

Struengmann teaches that meloxicam is a new NSAID with high anti-inflammatory potency and low ulcerogenic activity and low renal toxicity (pages 1- 2).

Thus, it would have been obvious to one of ordinary skill in the art to modify the nanoparticulate composition of Bosch to include meloxicam as an NSAID agent in view of the teachings of Plachetka or Struengmann. This is because Plachetka teaches that typical NSAIDs include meloxicam and naproxen, because Plachetka teaches both naproxen and meloxicam are known NSAIDs that provide long lasting analgesic effect, because Struengmann teaches meloxicam is a useful NSAID compound with fewer side effects, and because Bosch teaches a process suitable for any typical NSAIDs.

It is noted that Bosch does not explicitly teach the claimed properties such as the T_{max} or C_{max} values of the NSAID. However, the burden is shifted to applicant to show

that the nanoparticle obtained from Bosch does have the claimed properties, such as T_{max}, C_{max}, or any release profiles. This is because Bosch teaches the desirability for preparing a similar composition, namely, a stable, dispersible, water-insoluble drug nanoparticles comprising crystalline drug substance, such as an NSAID, having a surface modifier adsorbed on the surface thereof.

Claims 18-25, 43-49 and 68-72 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bosch et al., in view of Desai et al. WO 01/45706 A1 or Courteille et al. US 5,384,124.

Bosch is relied upon for the reasons stated above. Bosch does not teach the second particle population.

Desai teaches a dual-release composition of low water soluble drug (COX-2 inhibitor) comprising first fraction of the drug in nano-particulate form having average diameter of about 200 to about 400 nm and a D90 particle size less then about 5 μm (page 18); and a second fraction of the drug in micro-particulate form having D_{10} particle size of between 25 to about 100 μm (page 20, 1st paragraph). The first fraction nano-particle drug can be present alone or in combination with one or more excipient, such as nano-particles of the drug have a surface modifying agent (PEG-400) adsorbed on the surface thereof (page 18, 3rd through page 19). The weight ratio of the first to the second fraction of the drug in the composition is about 1:10 to about 10:1 (page 22, 3rd paragraph). The composition can be in an oral dosage form including tablet, pills, hard or soft capsule, lozenges, cachets, dispensable powder, granule, suspension or elixir (pages 37-38).

Courteille teaches a solid unitary composition comprising combination of nano-particle having diameter of less than 1 μm and micro-particle having diameter of between 1 μm to 2 mm (see abstract, column 2, lines 32-46). The mixture of nano/micro-particle contains one or more active agents of the same or different type (column 1, lines 66-68, and column 2, lines 23-31). The active agent can be selected from antibiotic, analgesic, tranquilizer, vitamins, and therapeutic agents for diseases of allergies, hormones, or gastrointestinal tract (column 5, lines 46-66). The mixture of nano/micro-particle is prepared by any known method (air-fluidized bed coating, turbine coating, simple extrusion, or micro-encapsulation) employing the use of a polymer or a macromolecular substance (surface stabilizer) selected from the group of cellulose derivatives, starch, polyamide, collagen, dextrin, gelatin, polyvinyl chloride or the like (column 2, lines 46-55, and column 3, lines 18-40). The mixture further comprises stabilizing agent, surfactant, and biding agent (column 4, lines 20 through column 5, lines 1-28). Courteille further teaches the solid dosage form comprises immediate release with a secondary controlled release of mixture of nano/micro-particle (column 6, lines 16-50). The solid dosage form is to be incorporated into pharmaceutical oral dosage form (column 6, lines 51-56).

Thus, it would have been obvious to one of ordinary skill in the art to modify the composition of Bosch to include the second particle population in view of the teachings of Desai or Courteille, because Desai and Courteille teach compositions suitable for analgesic substance, because Desai and Courteille teach that combination of one or more population of active substance with different particle size is well known in the art,

and because Bosch teaches the desirability for obtaining a composition suitable for the treatment of conditions using NSAID active agents (column 8, lines 41-64).

Claim 30 is rejected under 35 U.S.C. 103(a) as being unpatentable over Bosch et al., in view of Stainmesse et al. US 5,133,908.

Bosch is relied upon for the reason stated above. Bosch does not teach dissolving the active substance in a solvent.

Stainmesse teaches a process for the preparation of dispersible colloidal systems of a substance in the form of nanoparticles, the process comprising: dissolving the substance in a solvent (step 1) (abstract; and column 2, lines 20-59; and column 3, lines 27-33). Thus, it would have been obvious to one of ordinary skill in the art to modify the process of Bosch using the precipitation techniques of Stainmesse, because Stainmesse teaches a process suitable for the production of nanoparticles smaller than 500 nm, and because Stainmesse teaches a process that exhibits only a slight variation in size (column 5, lines 1-23).

Response to Arguments

Applicant's arguments filed 12/22/08 have been considered but are moot in view of the new ground(s) of rejection.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to S. Tran whose telephone number is (571) 272-0606. The examiner can normally be reached on M-F 8:00 am to 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward can be reached on (571) 272-8373. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/S. Tran/
Primary Examiner, Art Unit 1618